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TITLE: The Effect of COX-2 Inhibitors on the Aromatase Gene Expression in Human Breast Cancer

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13. ABSTRACT (Maximum 200 Words)

Aromatase (CYP-19) is responsible for estrogen biosynthesis within breast tumor tissue. Aromatase and cyclooxygenase-2 (COX-2) are both overexpressed in human breast cancer, and increased levels of prostaglandin (PG) activates the CYP19 promotor and increases gene expression. We hypothesize that celecoxib, a selective COX-2 inhibitor, will decrease PG, decrease the expression of CYP19, and reduce estrogen biosynthesis within tumor tissue. To test this hypothesis, in DOD grant # DAMD17-01-1-0589, tumor tissue will be collected from breast cancer patients at the initial diagnosis, and again at the definitive surgery (lumpectomy or mastectomy) for breast cancer. In the 10-14 day interval before the definitive surgery, patients will receive celecoxib and tissue samples collected before and after treatment with celecoxib will be evaluated for gene expression of COX-2 and CYP19. If our hypothesis is correct, then expression of the CYP19 gene will decrease in response to celecoxib. This study will provide preliminary data to a) support a mechanism whereby COX-2 inhibitors decrease estrogen production within breast tumors by decreasing CYP19 expression; and b) provide the rationale for initiating larger chemoprevention and therapeutic trials of COX-2 inhibitors in high risk and breast cancer patients.

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INTRODUCTION

This study will test the hypothesis that celecoxib, a selective Cox-2 inhibitor, will decrease PG, decrease the expression of CYP19, and reduce estrogen biosynthesis within tumor tissue. The primary objective of the study is to evaluate Aromatase (CYP19) and estrogen receptor (ER) gene expression by reverse-transcriptase polymerase chain reaction (RT-PCR) in response to a selective cyclooxgenase-2 (COX-2) inhibitor, celecoxib, in paired tumor tissue collected at the time of the initial diagnosis and at the time of definitive surgery for localized, non-metastatic breast cancer patients. The secondary objective is to evaluate the effect of celecoxib on the following biomarkers: estrogen receptor, progesterone receptor, Her-2/neu, Ki-67, COX-1, COX-2, CYP19, CD31, and PGE2, and Aromatase activity in paired tissue specimens by standard immunohistochemical methods. The study has been approved by both The Ohio State University IRB and the Army. In total, 34 subjects will be enrolled on the study. We anticipate that all 34 patients will be enrolled by May 31, 2004. The Army approved an extension to the performance period in March 2003. The performance period is now June 1, 2001 - June 30, 2004 (research to be completed by May 31, 2004).

BODY

Study staff began to screen for potential subjects in May 2003. As of May 31, 2003, no subjects were enrolled on the study.

KEY RESEARCH ACCOMPLISHMENTS

Not applicable. No patients have been enrolled on the study.

REPORTABLE OUTCOMES

Not applicable. No patients have been enrolled on the study.

CONCLUSIONS

Not applicable. No patients have been enrolled on the study.

REFERENCES

Not applicable. No patients have been enrolled on the study.

APPENDICES

Not applicable. No patients have been enrolled on the study.